

# Characterization of interventricular desynchronization in heart failure patients

K. Rotter<sup>1</sup>, K. Kroll<sup>1</sup>, C. A. Nienaber<sup>1</sup>, B. Ismer<sup>2\*</sup>

<sup>1</sup> University Hospital Rostock, Center for Internal Medicine I, Rostock, Germany

<sup>2</sup> Peter Osypka Institute for Pacing and Ablation at Offenburg University of Applied Sciences, Offenburg, Germany

## Abstract

Currently, QRS width and bundle branch block morphology are used as electrocardiographic guideline criterias to select heart failure (HF) patients with interventricular desynchronization in sinus rhythm (SR) for cardiac resynchronisation therapy (CRT). Nevertheless, up to 30% of these patients do not benefit from implantation of CRT systems. Esophageal left ventricular electrogram (LVE) enables semi-invasive measurement of interventricular conduction delays (IVCD) even in patients with atrial fibrillation (AF). To routinely apply this method, a programmer based semi-invasive automatic quantification of IVCD should to be developed. Our aims were to define interventricular conduction delays by analyzing fractionated left ventricular (LV) deflections in the esophageal left ventricular electrogram of HF patients in SR or AF.

In 66 HF patients (49 male, 17 female, age  $65 \pm 10$  years) a 5F TOslim electrode (Osypka AG, Germany) was perorally applied. Using BARD EP Lab, cardiac desynchronization was quantified as interval IVCD between onset of QRS in surface ECG and the investigator-determined onset of the left ventricular deflection in LVE. IVCD was compared with the intervals between QRS onset and the first maximum (IVCD<sub>m1</sub>) and between QRS onset and the second maximum (IVCD<sub>m2</sub>) of the LV complex.

QRS of  $173 \pm 26$  ms was linked with empirical IVCD of  $75 \pm 25$  ms, at mean. First and second LV maximum could be ascertained beyond doubt in all patients. Significant correlations of the  $p < 0,01$  level were found between IVCD and the IVCD<sub>m1</sub> of  $96 \pm 28$  ms as well as between IVCD and the IVCD<sub>m2</sub> of  $147 \pm 31$  ms, at mean.

To standardize automatic measurement of interventricular conduction delays with respect to patients with fractionated LV complexes, the first maximum of the LV deflection should be utilized to qualify the IVCD of HF patients with sinus rhythm and atrial fibrillation.

## Introduction

Heart failure is one of the most frequent diseases in Europe. The number of patients is estimated to be more than 10 million people [1]. In about 30% the reason is based on desynchronization between the left and right ventricular contraction [2]. In this cases, Cardiac Resynchronization Therapy (CRT) is an established concept to soften the symptoms and to increase the patients quality of life, as well as to reduce disease-associated complications and sudden death [3].

Unfortunately, despite using guideline criterias [4], up to one third of the patients do not clinically benefit from implantation of biventricular pacing systems [2]. Patient selection may be only one of the reason for this high non-responder rate. Using QRS width and bundle branch block morphology, extent of the interventricular conduction delay can be determined indirectly. Standard echocardiography and tissue Doppler imaging (TDI) do not allow a certain determination and quantification of interventricular desynchronisation as results of these methods are restricted by low accordance between the different measurement techniques. This explains the farther seeking for robust and reproducible

echocardiographic markers to predict individual CRT-response [5].

In addition to the above mentioned methods, the transesophageal left ventricular electrogram (LVE) provides a more direct, semi-invasive parameter of the left ventricular conduction delay [6]. It can be used to quantify the interventricular desynchronization in patients with sinus rhythm as well as in atrial fibrillation [7, 8]. Thus, it could be used as an additional method to select patients eligible for implantation of CRT systems (figure 1). The preoperatively quantified esophageal interventricular conduction delay (IVCD) could also be used intraoperatively to guide the left ventricular electrode placement. Thus, it supports locating the best possible electrode position in order to improve the CRT responder rate.

---

\*Corresponding author: Bruno Ismer, Peter Osypka Institute for Pacing and Ablation at Offenburg University of Applied Sciences, Badstrasse 24a, 77652 Offenburg  
E-mail: poi@hs-offenburg.de

## Aims

At present, manual measurement is the only way to ascertain transesophageal interventricular conduction delays. Therefore, the investigator has to determine the onset of the left ventricular deflection, even in cases with fractionated left ventricular complexes. To exclude investigator related inaccuracies and to routinely apply this method, a software or programmer based automatic quantification of the IVCD should be developed.

To enable reproducible determination of interventricular conduction delays in patients with sinus rhythm or atrial fibrillation, even with fractionated left ventricular deflection, our aim was to define parameters of the esophageal left ventricular electrogram that correlate within a high rate to IVCD and in the same time are reliable to register by automatic analyzing programmes.

## Patients and Methods

In 60 heart failure patients in sinus rhythm and 6 in atrial fibrillation (49 male, 17 female, age  $65 \pm 10$  years), an esophageal 5F TOslim electrode (Osypka AG, Rheinfelden, Germany) was perorally applied in position of the maximal left ventricular deflection. Esophageal left ventricular electrogram was recorded simultaneously with surface ECG. Therefore, the TOslim electrode was connected via the Esophageal Rostock Filter (Osypka AG, Rheinfelden, Germany) to the BARD EP Lab. This combination enables a Butterworth 15 Hz high-pass filtering of the bipolar esophageal left ventricular electrogram.



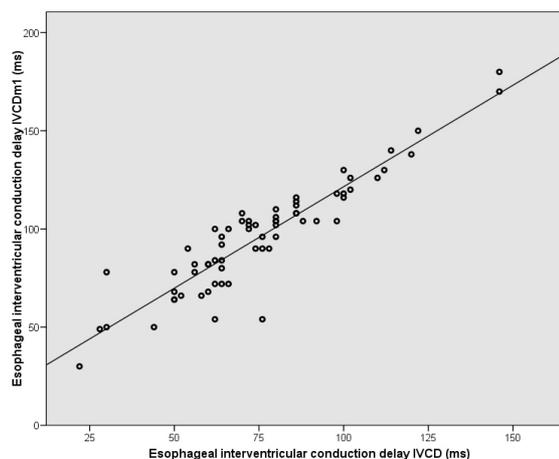
**Figure 1:** Measurement of interventricular conduction delay IVCD by LVE feature in the Biotronik ICS3000 programmer: Caliper 1 is set on first QRS onset in surface ECG, caliper 2 marks the beginning of the left ventricular deflection in LVE.

Cardiac desynchronization was quantified by two different measurements of the interventricular conduction delay. At first, the calliper was fixed to the QRS onset in surface ECG. Then, IVCD was determined by the investigator-determined onset of the left ventricular deflection in the LVE. Additionally,  $IVCDm_1$  and

$IVCDm_2$  were characterized ending with the first and the second positive or negative maximum of the left ventricular deflection, respectively.

## Results

Application of the esophageal electrode was well tolerated by all of the 66 patients. QRS width in surface ECG was  $173 \pm 26$  ms, at mean, with minimum of 104 ms and maximum of 242 ms. It was linked with IVCD of  $75 \pm 25$  ms, ranging between 22 and 146 ms. The correlation of QRS and IVCD was found to be significant at the  $p < 0,01$  level.



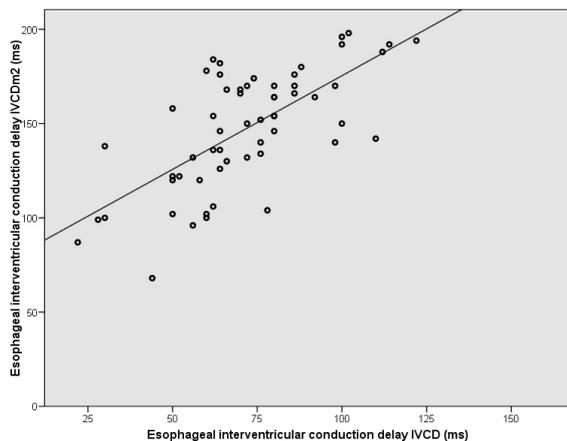
**Figure 2:** The correlation between IVCD, measured from QRS onset in surface ECG to the beginning of the left ventricular deflection in LVE and  $IVCDm_1$ , our proposed marker for IVCD in a automatic analyzation, defined as intervall between QRS onset and the first positive or negative peak value in LVE, is shown significant at the  $p < 0,01$  level.

The first and second left ventricular maximum or minimum could also be ascertained without doubt in all patients. Significant correlations at the  $p < 0,01$  level were also found between IVCD and  $IVCDm_1$  (figure 2) and between IVCD and  $IVCDm_2$  (figure 3).  $IVCDm_1$  differed from 30 to 180 ms with a mean of  $96 \pm 28$  ms and  $IVCDm_2$  was  $147 \pm 31$ , at mean, ranging between 68 and 198 ms.

## Conclusions

The extent of cardiac desynchronization has been proven to be a highly correlating parameter for reverse remodelling and quality of life in heart failure patients after implantation of CRT systems [9]. Esophageal left ventricular electrogram offers an easy and timesaving method to quantify the interventricular conduction delay more directly than via QRS width in surface ECG. The

preoperatively measured IVCD also provides a quality marker of the left ventricular electrode position. It indicates the minimal electrical delay that should be reached during the electrode placement. In patients with antero-lateral dyssynchrony it might not detect the maximal desynchronization due to esophagus anatomy which is strictly related to the posterior wall of the left ventricle. Nevertheless, if the esophageal left ventricular delay exceeds the delay measured via left ventricular electrode, the search for better position should be continued.



**Figure 3:** IVCD<sub>m2</sub>, measured between QRS onset in surface ECG and the second positive or negative peak value in LVE, is also significantly correlating with IVCD.

As a first step towards a routinely utilization of transesophageal electrogram, upon our request, a left heart electrogram feature was implemented into the Biotronik ICS3000 programmer (Biotronik, Berlin, Germany) [11]. It allows recording and calliper measurement of the esophageal electrogram in combination with 3-channel surface ECG in patients without or with CRT systems irrespective of make and model. In patients carrying Biotronik systems, the esophageal electrogram can be compared with telemetric right atrial and right and left ventricular electrograms.

To automate IVCD measurement in heart failure patients with sinus rhythm and atrial fibrillation, we propose the utilization of IVCD<sub>m1</sub> measured between QRS onset and the first positive or negative maximum of the left ventricular deflection, especially in patients with fractionated left ventricular deflection. IVCD<sub>m2</sub> also correlates with IVCD at a high level, but the coefficient is higher in IVCD<sub>m1</sub>. Additional peak values (IVCD<sub>m3</sub>, IVCD<sub>m4</sub> etc.) are not advantageous as the correlation decreases and they don't exist in unfractionated left ventricular complexes any more.

Thus, larger studies with a higher number of patients have to follow in order to define quantitative values for IVCD<sub>m1</sub> as a parameter determining interventricular dyssynchrony and as an indicational value for biventricular pacing systems.

## References

- [1] Hoppe U. C., Böhm M., Dietz R., Hanrath P., Kroemer H. K., Osterspey A., Schmaltz A. A., Erdmann E., in Zusammenarbeit mit der Arzneimittelkommission der Deutschen Ärzteschaft: Leitlinien zur Therapie der chronischen Herzinsuffizienz; *Z Kardiol* 94, 488-509 (2005)
- [2] Abraham W. T., Fisher W. G., Smith A. L., Delurgio D. B., Leon A. R., Loh E., Kocovic D. Z., Packer M., Clavell A. L., Hayes D. L., Ellestad M., Messenger J.; MIRACLE Study Group: Cardiac Resynchronization in Chronic Heart Failure; *N Engl J Med*, 346(24), 1845-1853 June 13 (2002)
- [3] Cleland J. G. F., Daubert J. C., Erdmann E., Freemantle N., Gras D., Kappenberger L., Tavazzi L., for the Cardiac Resynchronization – Heart Failure (Care-HF) Study Investigators: The Effect of Cardiac Resynchronization on Morbidity and Mortality in Heart Failure; *N Engl J Med*, 352(15), 1539-1549 April 14 (2005)
- [4] Vardas P. E., Auricchio A., Blanc J. J., Daubert J. C., Drechsler H., Ector H., Gasparini M., Linde C., Morgado F. B., Oto A., Sutton R., Trusz-Gluzza M., developed in Collaboration with the European Heart Rhythm Association: Guidelines for cardiac pacing and cardiac resynchronization therapy; *European Heart Journal* (2007) 28, 2256-2295
- [5] Burri H., Müller H., Vieira I., Lerch R.: Poor agreement of echographic measures of ventricular dyssynchrony; *European Journal of Echocardiography* (2008) 9, 235-240
- [6] Heinke M., Surber R., Kühnert H., Dannberg G., Prochnau D., Figulla H. R.: Transesophageal left ventricular posterior wall potential in heart failure patients with biventricular pacing; *Biomed Techn* (2007) 52, 173-179
- [7] Heinke M., Ismer B., Kühnert H., Figulla, H. R.: Transesophageal left ventricular electrogram recording and temporary pacing to improve patient selection for cardiac resynchronization; *Med Biol Eng Comput* (2011) 49, 851-858
- [8] Kroll K., Ismer B., Heinke M., Rotter K., Akin I., Schell-Dieckel S., Trautwein U., Melzer C., Weber F., Nienaber C. A.: Programmer ICS3000 esophageal left heart electrogram feature to measure interventricular and intra-left-ventricular conduction delay in CRT patients; *J Interv Card Electrophysiol* 27 (2010) 3, 212-213
- [9] Gold M. R., Birgersdotter-Green U., Singh J. P., Ellenbogen K. A., Yu Y., Meyer T. E., Seth M., Tchou P. J.: The relationship between ventricular

electrical delay and left ventricular remodelling with cardiac resynchronization therapy; *European Heart Journal* 32 (2011), 2516-2524

- [10] Ismer B., von Knorre G. H., Voß W., Placke J.: Approximation des individuell optimalen AV-Delays mittels linksatrialer Elektrokardiographie; *Herzschr Elektrophys* 15:Suppl 1 I/33-I/38 (2004)
- [11] Ismer B., Körber T., von Knorre G. H., Voß W., Weber F., Melzer C., Peters R., Nienaber C. A.: Utilization of ICS3000 programmer to measure interatrial conduction intervals and to optimize the AV-delay in patients with biventricular pacemakers and ICDs irrespective of make and model; *Europace* 7 (2005), 290